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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,659	06/14/1999	FREDERIC ZENHAUSERN	4467-102US	3190

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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9M.

Office Action Summary	Application No. 09/332,659	Applicant(s) ZENHAUSERN, FREDERIC	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-7,9,10,12-14,42 and 45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-7,9,10,12-14,42 and 45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 20 May 2004 in which claims 1 and 45 were amended. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 5 March 2004, not reiterated below, are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection, necessitated by amendment, are discussed.

The complete listing of Claims does not comply with 37 C.F.R. 1.121 because the listing does not identify all claims 8, 11, 43 and 44 as being canceled. It is noted that these claims were canceled in papers filed 9 September 2003.

Claims 1, 4-7, 9-10, 12-14, 42 and 45 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 4-7, 9-10, 12-14, 42, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-7, 9-10, 12-14, 42, and 45 are indefinite in Claim 1 because the claim is drawn to a method for directly monitoring volatile compounds from a nucleic acid enzymatic

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reaction. However, the method steps of the claim do not include any enzymatic reactions. Hence it is unclear whether claimed method monitors an enzymatic reaction as claimed. Furthermore, absent an enzymatic reaction, it is unclear how or whether monitoring occurs during the reaction as recited in the preamble of the claim. While the claim recites "screening the medium...so that more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detected..", the method steps do not recite a catalyst or active step producing the detectable change.

Claim 42 is indefinite for the recitation "the enzymatic biomolecular reaction" because the recitation lacks proper antecedent basis in Claim 1.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 7, 9-10, 12-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997).

Regarding Claim 1, Van Ness et al disclose a method for monitoring a reaction comprising the steps of attaching one or more volatile organic tags a nucleic acid (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-

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chemical change of a gas or vapor phase of a nucleic acid is detected (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, (Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information “representative” of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33). The instant specification broadly defines the “multisensor array” at pages 21-23 as being at least two different sensors (page 21, line 20). Van Ness et al teach numerous sensors including embodiments wherein the multisensor array comprises multiple mass spectrometer detectors (Column 64, lines 44-47) of a quadrupole mass analyzer (Column 59, lines 1-22 and Column 67, lines 6-10). Hence, Van Ness et al teach the multisensor array as claimed.

The claim is drawn to a method for directly monitoring volatile compounds in a gas or vapor phase from a nucleic acid enzymatic reaction during the reaction. However, as stated above the method steps do not include steps of enzymatic reactions. Furthermore, the claim does not define time range encompassed by the recitation “during the reaction”. As cited above, Van Ness et al disclose the claimed method steps. Van Ness further teach detection of an enzymatic reaction i.e. cleavage (Column 55, lines 54-57) and they teach numerous examples of screening the medium during the cleavage reaction as claimed (Columns 69-70).

Regarding Claim 7, Van Ness et al disclose the method wherein the multisensor array comprises at least one of a vibrating (Column 57, line 65-Column 58, line 8) or resonant micromechanical device (Column 60, lines 2-23).

Regarding Claim 9, Van Ness et al disclose the method wherein the multisensor array comprises a mass spectrometer (Column 59, lines 1-22).

Regarding Claim 10, Van Ness et al disclose the method wherein the multisensor array comprises an optical sensing probe (Column 63, lines 50-57).

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Regarding Claim 12, Van Ness et al disclose the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid (Column 67, lines 1-28).

Regarding Claim 13, Van Ness et al disclose the method wherein the information includes a change in the concentration of nucleic acids i.e. cleavage of the tag from the nucleic acid (Column 63, lines 1-50).

Regarding Claim 14, Van Ness et al disclose the method wherein the information includes a change in at least one secondary product of the reaction i.e. cleavage of the tag (Column 63, lines 12-23).

Response to Arguments

6. Applicant argues that Van Ness requires separation of the nucleic acid fragments prior to detection and hence does not teach the instant invention of directly monitoring a nucleic acid enzymatic reaction during the reaction. The argument has been considered but is not found persuasive. The fact that Van Ness separates fragments prior to cleavage does not alter the fact that they monitor enzymatic cleavage thereby meeting the limitations of the claims. Additionally, as stated above, the instant claims do not recite method steps of monitoring a nucleic acid reaction during the reaction. While the preamble includes the recitation of monitoring... during the reaction, the preamble does not define a time period encompassed by the recited "during" nor does the preamble define or limit the enzyme. Hence, the cleavage (enzymatic) monitoring of Van Ness is encompassed by the claimed method. Applicant asserts that the instant invention is drawn to a real time method for directly monitoring an enzymatic reaction, during the reaction. However, the method steps do not include "real time", "directly monitoring" or "monitoring during the reaction". Hence, the arguments are not commensurate in scope with the claims.

7. Claims 1, 7, 9, 12-14, 42 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Koster et al (U.S. Patent Application Publication No. 2002/0009394, filed 2 April 1999).

Regarding Claim 1, Koster et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product, screening the medium with a multisensor array (§ 81) whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable to provide information to produce a signal output, transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means, sorting the information in accordance with a set of class boundaries and monitoring the information "representative" of the identity and amount of nucleic acid (§ 108-125).

Regarding Claim 7, Koster et al disclose the method wherein the multisensor array comprises a resonant micromechanical device (i.e. FTICR, § 81).

Regarding Claim 9, Koster et al disclose the method wherein the multisensor array comprises a mass spectrometer (§ 81).

Regarding Claim 12, Koster et al disclose the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid (§ 132-133).

Regarding Claim 13, Koster et al disclose the method wherein the information includes a change in the concentration of nucleic acids e.g. expression which determines concentration in the cell (e.g. § 5) or following PCR which determines changes of concentration i.e. amplification (§ 86).

Regarding Claim 14, Koster et al disclose the method wherein the information includes the a change in at least one secondary product of the reaction i.e. ionization (§ 110-119)

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Regarding Claim 42, Koster et al disclose the method wherein the reaction is PCR (e.g. ¶ 86).

Regarding Claim 45, Koster et al disclose the method further comprising controlling the PCR reaction i.e. computer controlled thermocycler (¶ 94-97).

Response to Arguments

8. Applicant asserts “for an asserted reference to anticipate a claimed invention, that reference must also teach how to make and use at least one embodiment within the scope of the claims at issue”. Applicant further asserts “Koster ('394) as a matter of law, cannot anticipate any of the claims to the present invention.” Applicant assertions are acknowledged. However, the examiner is unaware of any statutes requiring that a reference disclose an embodiment within the scope of the claimed invention. 35 U.S.C. 102 (e) requires:

A person shall be entitled to a patent unless –

(e) **the invention was described** in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

As cited above, Koster clearly describes the invention as instantly claimed. Hence, the instant claims are anticipated by Koster as defined by 35 U.S.C. 102(e).

Applicant argues that although Koster contemplates biopolymer analysis, the “all encompassing language throughout the specification does not describe or enable an embodiment that falls within the scope of the instantly claimed invention. The argument has been considered but is not found persuasive. The courts have stated that a reference contains an “enabling disclosure” if the public was in possession of the claimed invention before the date of invention. “Such possession is effected if one of ordinary skill in the art could have combined

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the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985) (MPEP § 2121.01). Hence, the teaching of Koster is deemed enabling.

Applicant further argues that Koster does not contemplate using a "real time single-stop multisensor array in a gas or vapor phase medium of a nucleic acid reaction". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., real time single-stop multisensor array) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Freidhoff et al (U.S. Patent No. 5,386,115, issued 31 January 1995).

Regarding Claims 4-6, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a

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multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al further teach the method wherein the sensor comprises anyone of many known in the art (e.g. Column 64, line 48-Column 65, line 19) but they do not specifically teach the sensor comprises a semiconductor gas sensor (Claim 4); a metal oxide gas sensor (Claim 5); or a conductive polymer sensor (Claim 7). However, the claimed sensors were well known in the art at the time the claimed invention was made as taught by Freidhoff et al who teach their multisensor array (Fig. 1) comprising a semiconductor gas sensor (Column 3, lines 47-57) comprising a metal oxide gas sensor (Column 5, lines 39-54) and comprising a conductive polymer sensor (i.e. electrodes of conductive material, Column 5, lines 7-17). Freidhoff et al teach their semiconductor gas sensor is small, low power, easily transportable and has the ability to detect multiple constituents simultaneously thereby providing a low cost sensor having wide applications (Column 2, lines 25-30).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sensor of Freidhoff et al to the gas sensor in the method of Van Ness et al based on the preferred teaching and advantages taught by Friedhoff et al. Specifically, one of ordinary skill would have been motivated to use the small, low power, easily transportable sensor of Friedhoff et al for the expected benefits of providing a low cost sensor having wide applications (Column 2, lines 25-30).

Response to Arguments

11. Applicant argues reiterates the arguments that Van Ness requires a separation step not required in the instant claims. The argument has been considered but not found persuasive because as stated above the enzymatic cleavage of Van Ness is encompassed by the instant claims and further because the method steps do not include method steps limiting the inclusion of separation.

Applicant further argues that while Van Ness and Koster could have added the elements taught by Freidhoff, neither incorporated those elements into their disclosure. Hence, Applicant assert, the combination was not contemplated by one of skill in the art. Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

12. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Koster et al (U.S. Patent Application Publication No. 2002/0009394, filed 2 April 1999).

Regarding Claim 45, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means

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(software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information “representative” of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al teach the method wherein the reaction is PCR (e.g. Column 18, lines 21-29 and Column 65, lines 64-67) but they do not specifically teach controlling the PCR. However, it was well known in the art at the time the claimed invention was made that PCR is routinely performed by repeated cycles of high and low temperatures controlled by a thermocycler (see Koster et al: ¶ 94-97). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to control the PCR in the method of Van Ness et al based on the well known use of thermocyclers for PCR as taught by Koster et al (¶ 94-97) for the obvious benefit of using routinely practiced methods to thereby obtain desired results i.e. amplification.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

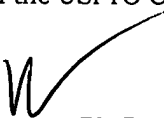
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
July 27, 2004